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Severe Cysticercal Meningitis: Clinical and Imaging Characteristics

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Abstract. In disease-endemic areas, severe cysticercal meningitis (SCM) is characterized by intense inflammatory cerebrospinal fluid (CSF) and negative bacterial and fungal cultures. There have been no systematic studies of SCM. We characterized patients with SCM and compare them with neurocysticercosis (NC) patients with mild CSF abnormalities by conducting a nine-year retrospective review at a neurological referral center. Two groups of patients were compared: group A, those with severe CSF pleocytosis > 1,000 cells/mm^3 (n = 12), and group B, those with CSF pleocytosis ≤ 1,000 cells/mm^3 (n = 126). All patients had positive CSF results in an enzyme-linked immunosorbent assay for cysticercal antigens and negative CSF cultures for bacteria, fungi, and mycobacteria. Intracranial hypertension, meningeal signs, CSF hypoglycorrachia, and a longer clinical course of NC were more frequently seen in group A. It is likely that SCM often goes unrecognized. Its correct identification may reduce morbidity and risks of unnecessary surgery in patients with chronic NC and CSF shunts.

INTRODUCTION

Clinical manifestations of neurocysticercosis (NC), the invasion of the central nervous system by the metacestode of *Taenia solium*, are variable and closely associated with the topography, number and stage of parasites, and the intensity of the immuno-inflammatory response. These factors produce pleomorphic clinical, radiological, and cerebrospinal fluid (CSF) inflammatory changes.[1] The most severe forms of NC occur when parasites are located in the subarachnoid space at the base of the brain or in the ventricular system.[2,3] Subarachnoid locations seem to be more frequent in Latin America, and soft tissue locations seem to be more common in Asia and Africa.[4]

Cysticercal meningitis is a term without well-defined diagnostic criteria. When parasites lodge in the subarachnoid space at the base of the brain, a mild or moderate CSF inflammatory profile (< 500 cells/mm^3) is observed.[4–8] In some cases, cellularity is higher, reaching ≥ 1,000 cells/mm^3. This condition presents a diagnostic challenge because of the need to discriminate this entity from acute superimposed bacterial meningitis, especially if a CSF shunt has been previously placed. The first medical approach for these patients is generally to remove the shunt on the basis of the possibility of a bacterial infection, which unnecessarily exposes the patient to the risks of surgery with an increase in morbidity and costs.

In this report, we describe a series of patients with severe cysticercal meningitis (SCM). We compared their clinical, radiological, and CSF inflammatory characteristics with another group of patients with subarachnoid parasites who had a less intense CSF inflammatory reaction.

METHODS

A retrospective analysis was conducted of patients with a discharge diagnosis of NC who were hospitalized at a reference Neurological Center in Mexico City (Instituto Nacional de Neurología y Neurocirugía Manuel Velasco Suárez) during January 1998–December 2007. The diagnosis of NC was based on clinical and imaging data, residence in an disease-endemic area, and a positive result in an enzyme-linked immunosorbent assay for cysticercal antigens in CSF.[9] Only patients with subarachnoid NC were included.

Patients were divided into two groups. Group A consisted of patients who had CSF cell counts > 1,000 cells/mm^3, and group B of patients consisted of patients who had CSF cell counts ≤ 1,000 cells/mm^3. The lowest cell count considered was 10 cells/mm^3. We made this arbitrary division because 1,000 cells/mm^3 is considered the set point for pyogenic etiology, which was the first differential diagnosis to be considered in these patients.

All patients included had repeatedly negative CSF cultures for bacteria, fungi, and mycobacteria; negative polymerase chain reaction results for *Mycobacterium tuberculosis*; and negative latex agglutination test results for cryptococcal polysaccharide. Categorical variables were compared with Fisher's exact test and continuous variables were compared with Student's *t*-test.

RESULTS

A total of 6,181 patients were hospitalized in our center during this period. Of these patients, 336 (5.44%) had NC and 138 (41%) had parasites in the subarachnoid space at the base of the brain.

Group A had 12 patients (8.7%) with CSF pleocytosis > 1,000 cells/mm^3, and group B had 126 patients (91.3%) with pleocytosis ≤ 1,000 cells/mm^3. Differences in clinical, radiological, and CSF inflammatory profiles are summarized in Table 1.

Patients with a severe CSF inflammatory response (group A) showed a chronic history of NC with a mean ± SD disease duration of 36.33 ± 13.4 months (range = 6–168 months), and patients in group B had a mean ± SD disease duration of 15.6 ± 1.91 months (range = 1–138 months) (P = 0.001). The more common clinical manifestations in group A were intracranial hypertension (ICH) in nine patients and meningeal signs in five patients; other symptoms were headache and epilepsy. In group B, ICH was present in 90 patients, meningeal signs in 14, headache in 9, and motor deficit in 7. The remaining patients had mixed symptoms.

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TABLE 1
Characteristics of study participants, Mexico*

Characteristics	Group A (n = 12)	Group B (n = 126)	*P*
Mean ± SD age, years	38.17 ± 3.46	38.7 ± 1.2	0.6
Place of origin, no. (%)			
Rural	4 (33.3)	9 (0.7.1)	
Urban	8 (66.6)	117 (92.8)	1
Sex, no. (%)			
F	3 (25)	57 (44.4)	
M	8 (75)	70 (55.6)	0.2
Clinical features, no. (%)			
Papilledema	9 (75)	90 (70.9)	1
Meningeal signs	6 (50)	14 (11.2)	0.001
Recurrent NC	4 (33.3)	52 (40.9)	0.7
Mean ± SD months of NC evolution before SCM	36.33 ± 13.4	15.66 ± 1.90	0.001
CSF inflammatory characteristics			
Pleocytosis, mean ± SD (%)			
Lymphocytes, cells/mm^3	1,398 ± 584.75 (32)	90.65 ± 11.79 (90)	0.001
Neutrophils, cells/mm^3	2,157.75 ± 475.78 (64)	23.53 ± 7.8 (10)	0.001
Eosinophils, cells/mm^3	2.3 ± 2	2.45 ± 1.4	0.16
Proteins, mg/dL	262.36 ± 79.23	172.41 ± 33.36	0.3
Glucose, mg/dL	20.36 ± 5.97	45.35 ± 2.32	0.001
Radiological features, no. (%)			
SA or IV vesicular parasites	10 (83.3)†	119 (93.7)	0.2
Colloidal parasites	1 (8)	15 (13.8)	1
Calcified parasites	10 (83.3)	39 (31.5)	0.002
Mass effect by vesicular cysticerci	5 (41.7)	103 (82)	0.02
Basal meningeal enhancement	6 (50)	36 (28)	0.02
Ependymitis	2 (16)	21 (16)	0.8
Hydrocephalus	11 (91.7)	93 (75)	0.3
Infarct or vasculitis	0	18 (14.4)	

* NC = neurocysticercosis; SCM = severe cysticercal meningitis; CSF = cerebrospinal fluid; SA = subarachnoidal; IV = intranventricular.
† One patient had only intraventricular ependymitis and another had a colloidal parasite no. (%) number and percentage.

In group A, five patients had a clinical episode of SCM associated with sudden suppression of chronic corticosteroid treatment. In one patient, SCM was associated with albendazole treatment. Nine patients (75%) in group A required a ventriculo-peritoneal shunt (VPS) compared with 64 (50.4%) patients in group B ($P = 0.09$). Ten patients (83.3%) in group A and 39 (31.5%) of group B also had parenchymal dead calcified parasites ($P = 0.002$). Basal meningeal enhancement was observed in imaging studies in 6 patients (50%) from group A and in 36 patients (28%) from group B ($P = 0.02$). Ischemic infarcts, probably associated to secondary small vessel vasculitis, were observed only in patients from group B.

In addition to CSF total cell counts, patients in group A had increased neutrophils with a mean ± SD of 2,158 ± 475.78 cells/mm^3 with a neutrophil:lymphocyte ratio of 2:1, lower glucose levels ($P < 0.001$), and a non-significant tendency for higher protein levels ($P = 0.3$). We do not consider a set point on the basis of CSF glucose level because there are patients with low glucose levels in CSF who have normal or minimal increased cell counts with minimal or no symptoms, especially if they are receiving oral corticosteroids. The mean ± SD time of normalization of CSF pleocytosis was 5.89 ± 2.18 months (range = 0–18 months) in group A and 20.45 ± 4.77 months in group B ($P < 0.001$).

Patients with episodes of SMC were treated with corticosteroids. Specific anti-helminthic drugs such as albendazole or praziquantel were not administered so as to prevent intensification of the inflammatory response.[10,11]

On a Medline search with key words "acute and chronic cysticercal meningitis or meningoencephalitis," 15 reports and 3 series (63 patients) were obtained and summarized in Table 2. The diagnoses used as criteria for SCM in these reports were not uniform. All had CSF inflammatory profiles associated with meningeal signs in some patients and only 4 (6.3%) patients had SCM according to our criteria.

Clinical manifestations were variable: meningitis in 29 (46.7%), ICH in 24 (38.7%); and headache in 14 (22.5%). VPS was present in 4 (6.3%). Parenchymal parasites were found in 20 (32.2%), subarachnoid vesicles in 6 (9.6%), and basal meningeal enhancement in 2 (3.22%). A CSF inflammatory profile showed a mean ± SD low glucose level of 21 ± 5 mg/dL, a mean ± SD protein level of 203 ± 58 mg/dL, and a mean ± SD pleocytosis of 503.5 ± 183.5 cells/mm^3 (range = 12–3,025 cells/mm^3).

Treatment of patients was variable. Antibiotics were administered initially when bacterial meningitis was suspected, and corticosteroids were administered when acute symptoms of meningitis were present. Later, when a compatible CSF profile and a computed tomography scan showing NC were observed, albendazole or praziquantel was administered and patients showed apparent clinical improvement.[12,13] In other patients with chronic NC, contradictory results have been found.[14–16]

DISCUSSION

SCM is a term without proper classification and diagnostic criteria and includes wide CSF inflammatory variability. Abnormal CSF is reported in approximately 50% of patients with active NC.[22–25] The most common findings are a moderate mononuclear pleocytosis, with a cell count rarely exceeding 300 cells/mm^3,[3,7,8] a normal glucose level, although hypoglycorrhachia is seen in 12–18% of patients,[26–28] and a moderately increased level of CSF proteins (range = 50–300 mg/dL).[29,30]

TABLE 2

Summary of 15 cases and 3 series with severe cysticercal meningitis reported in the medical literature*

Case	Age, years/sex	Clinical manifestations	CSF characteristics						Radiological manifestations	Required surgery	Reference
			Glucose, mg/dL	Protein, mg/dL	Cells/mm^3	Neut, %	Lymph, %	Eosin, %			
1	3/M	AM	33.4	83	1,250	65	30	5	No abnormalities	No	12
2	19/M	Paraparesia	27	704	1,050	ND	ND	ND	Spinal arachnoiditis	No	14
3	33/M	Seizures	26	236	3,025	ND	ND	ND	SANC	Yes†	14
4	32/M	AM, SH	10	1,560	6,486	77	18	5	H, SANC, and hemorrhage	Yes‡	18
5	1/F	AM	39	40	560	70	30	ND	H and leptomeningitis	No	12
6	9/F	ME	45	610	950	90	10	ND	PP	No	13
7	42/M	ICH, visual alterations	0	148	53	ND	ND	ND	H and SANC	No	14
8	44/M	ICH	7.8	704	155	ND	ND	ND	H and SANC	No	14
9	45/M	ICH	16	90	129	ND	ND	ND	PP and SANC	Yes†	14
10	58/F	ICH	54	79	188	7	29	14	SANC, calcified and Me	No	15
11	44/M	ICH and AM	4	241	293	80	20		No abnormalities	ND	19
12	35/M	ICH	14	272	146	29	60	11	PP and SANC	Yes†	20
13	47/M	ICH	1.7	22.8	207	39	34	27	PP and H	ND	21
14	18/F	AM	ND	30	470	11	80	ND	Vesicular and calcified NC	No	22
15	24/M	Confusion, AM	30	120	190	10	90	–	PP and edema	No	23
Series											
1	M (n = 9), F (n = 6)	Headache 73%; visual alterations 93%; seizures 66%; meningeal signs 80%	ND	50–100	12–100	ND	ND	ND	In 9 patients multiple hypointense lesions and edema	ND	3
2	F (n = 1)/58, M (n = 5)/28–49	Headache 66%; gait alterations 83%; seizures 16%	19.5	21	40	ND	100	ND	H and infarcts	Yes†	16
3	M (n = 20)/4–52, F (n =7)/21–30	Fever 74%; meningeal signs 44%; ICH 72%; others 30%	ND	< 20 to > 75	< 20 to > 100		ND	ND	Suggestive lesions of NC in 6 patients	ND	17

*Neut = neutrophils; Lymph = lymphocytes; Eosin = eosinophils; AM = acute meningitis; ND = no data; SANC = subarachnoid neurocysticercosis; SH = subarachnoid hemorrhage; H = hydrocephalus; ME = meningoencephalitis; PP = parenchymal parasites; ICH = intracranial hypertension; Me = meningeal enhancement; AC = ; NC = neurocysticercosis.

†Ventriculoperitoneal shunt.

‡Ventriculostomy.

The pathophysiology of such a severe CSF response that mimics bacterial meningitis is unknown. A long course of NC with a high parasite load appears to be frequently seen in these patients; long-term duration of symptoms and calcified parasites were also more frequent in these patients. We speculate that in SCM, the predominance of neutrophils in CSF could be the consequence of expression of a neutrophil chemotactic factor, such as CXCL8/IL-8, which has been found at increased levels after *in vitro* monocyte and astrocyte stimulation by *T. solium* larval antigen.[31,32] Complementary immunological studies in NC are necessary to confirm this hypothesis.

The review of the medical literature about meningitis in NC confirms the infrequent occurrence of these severe forms; only four cases have been described. However, it is likely that SCM is often underdiagnosed and underreported.

According to our data, clinical manifestations of SCM seem to be heterogeneous; the clinical outcome was relatively benign in patients receiving corticosteroid treatment. There are no guidelines for specific management of SCM. We do not use antiparasitic drugs during episodes of SCM because it is well demonstrated that inflammation increases after such treatment because of parasite destruction and liberation of large concentrations of antigenic material.[10,11,33]

SCM seems to be an infrequent entity, but is probably underdiagnosed and underreported. It needs to be considered as a differential diagnosis from other forms of infectious meningitis in patients living in NC-endemic areas when compatible clinical data, imaging, and CSF inflammatory profiles, and negative bacterial and fungal cultures are found. Because of a high frequency of VPS in our patients with SCM, its correct identification, once bacterial infection is ruled out, may avoid unnecessary surgery that increases morbidity, risks, and treatment costs. Most patients improve clinically after treatment with corticosteroids; a complete normalization of CSF takes months.

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